AD	

Award Number: DAMD17-97-1-7355

TITLE: Illness Among Persian Gulf War Veterans: Case Validation

Studies

PRINCIPAL INVESTIGATOR: Bradley N. Doebbeling, M.D.

CONTRACTING ORGANIZATION: The University of Iowa

Iowa City, Iowa 52242-1320

REPORT DATE: October 1999

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command

Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;

Distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

20000105 061

REPORT DOCUMENTATION PAGE

rorm Approvea OMB No. 074-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, galhering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503

1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE	3. REPORT TYPE AND	DATES COVERE	D				
	-98 - 24-Se							
4. TITLE AND SUBTITLE	5. FUNDING N							
Illness Among Persian Gu	Validation	DAMD17-97-						
Studies	iii wai veterans. Case	validation	DAMDI J	1 7555				
Studies								
6. AUTHOR(S)								
Bradley N. Doebbeling, M.	I.D.							
7. PERFORMING ORGANIZATION NAM	ME(S) AND ADDRESS(ES)		8. PERFORMIN	G ORGANIZATION				
The University of Iowa			REPORT NU	MBER				
Iowa City, Iowa 52242-1320				•				
10.11 01.9, 10.11 022.12 1020				•				
E-MAIL:								
brad-doebbeling@uiowa.edu				•				
9. SPONSORING / MONITORING AGE	NOV NAME(C) AND ADDRESS(ES	<u></u>	10 CDONCODE	NO / MONITORING				
9. SPONSORING / MONITORING AGE	NCT NAME(5) AND ADDRESS(ES	·)	1	NG / MONITORING EPORT NUMBER				
			AGENCIA	EFORT NOWIBER				
U.S. Army Medical Research and M								
Fort Detrick, Maryland 21702-501	2							
11. SUPPLEMENTARY NOTES								
				·				
12a. DISTRIBUTION / AVAILABILITY S	STATEMENT			12b. DISTRIBUTION CODE				
Approved for public rele	ase; distribution unl	.imited						
13. ABSTRACT (Maximum 200 Words	;)							
We recently completed a popula	tion-based, cross-sectional te	elephone survey of 4	1,886 military p	ersonnel to compare the				
prevalence of self-reported symp								
during the Persian Gulf War (PG								
reported a significantly higher pr								
dysfunction, and fibromyalgia we								
exposures or other risk factors a								
The proposed investigations, a s								
	study, should provide an estimate of the true magnitude of the problem. Because of the magnitude of the difference in prevalence between these groups, it is critical to explore and characterize their cognitive deficits, depression, and							
multisystemic conditions. The primary purpose of the current project is to compare the true rate of confirmed disease								
among samples of veterans not deployed, with and without these self-reported conditions. Furthermore, we also plan to								
identify risk factors for each disease outcome of interest including medical and family history, psychological factors (such								
as major lifetime events or stress, personality traits, and social support), and occupational and environmental exposures								
for validated illness in a series of nested case-control studies.								
Year 2 of 4 the grant has just be	en completed. Through Sen	tember 1999, 155 sı	ubiects have he	een assessed, with a				
participation rate of 75%. Recruitment, assessment, and data collection, entry, and validation efforts are ongoing.								

NSN 7540-01-280-5500

OF REPORT

17. SECURITY CLASSIFICATION

Unclassified

18. SECURITY CLASSIFICATION

Unclassified

OF THIS PAGE

14. SUBJECT TERMS

Gulf War

Standard Form 298 (Rev. 2-89) Prescribed by ANSI Std. Z39-18 298-102

15. NUMBER OF PAGES

20. LIMITATION OF ABSTRACT

Unlimited

20 16. PRICE CODE

19. SECURITY CLASSIFICATION

Unclassified

OF ABSTRACT

FOREWORD

Opi	inior	ns, inte	erpre	etat:	ions	, conclusions	and	recomm	enda	tions	are	those
						necessarily						

____ Where copyrighted material is quoted, permission has been obtained to use such material.

Where material from documents designated for limited distribution is quoted, permission has been obtained to use the material.

____ Citations of commercial organizations and trade names in this report do not constitute an official Department of Army endorsement or approval of the products or services of these organizations.

N/A In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and use of Laboratory Animals of the Institute of Laboratory Resources, national Research Council (NIH Publication No. 86-23, Revised 1985).

 \underline{X} For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

N/A In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

N/A In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

N/A In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.

10-25-99

PI - Signatur

ate

Table of Contents

Foreword	iii
Introduction	1
Past Year's Progress Pilot Subjects Data Collection Instrument Revision Characteristics of Subjects Assessed to Date Data Analysis/Publication	1 2 2 4
Personnel	4
Research Methods	4
Research Subjects	5
Schedule	8
Data Management	8
Conclusion	9
List of Tables	
Table 1. Subjects Assessed Through 30 September 1999	3
Table 2. Total Cases and Controls Available for Assessment, Desired Sample Sizes, a Completed Subjects by <i>A Priori</i> Outcome Group Combinations	
List of Appendices	
Appendix A. Completed Assessments Broken Down by <i>A Priori</i> Outcome and Deployment Status (Assessments completed through 30 September 1999)	10
Appendix B. Recent PGW-Related Papers and Presentations	11
Appendix C. Study Personnel	13
Appendix D. Data Collection Instruments	14
Appendix E. Eligible Subjects (based on the study's three a priori outcomes)	16

DoD Annual Report October 1999

Illness Among Persian Gulf War Veterans: Case Validation Studies, Grant # DAMD17-97-1-7355

Introduction

We recently completed a population-based, cross-sectional/cohort telephone survey of 4,886 military personnel to compare the prevalence of self-reported symptoms and illnesses among military personnel either deployed, or eligible but not deployed, during the Persian Gulf War (PGW) (*JAMA*, 1997). The lowa Persian Gulf War Study, was originally funded by the Centers for Disease Control and Prevention. Compared with non-PGW military personnel, PGW military personnel reported a significantly higher prevalence of symptoms of a variety of conditions, although the frequency of *a priori* outcomes of depression, cognitive dysfunction, and fibromyalgia were particularly elevated. The validity of these outcomes and the existence of a causal relationship between either military exposures or other risk factors and documented illness for most symptomatic PGW veterans remains to be demonstrated.

This study, a series of case-validation and case-control studies nested within the previous population-based cohort study, should provide an estimate of the frequency of clinical illness. Because of the magnitude of the difference in prevalence between these groups, it is critical to explore and characterize the degree to which the groups exhibit cognitive deficits, depression, and fibromyalgia. The primary purpose of the current project is to compare the true rate of confirmed disease among samples of veterans deployed to the Gulf with and without these predefined conditions, versus true rate of confirmed disease among samples of veterans not deployed, with and without these self-reported conditions. Furthermore, we also plan to attempt to identify risk factors for each validated illness outcome of interest, including medical and family history, psychological factors (such as major lifetime events or stress, personality traits, and social support), and occupational and environmental exposures in a series of nested case-control studies.

Past Year's Progress

Pilot Subjects

Significant progress has been made in the past year. In late January 1999, seven members of the Iowa Army National Guard unit based in Iowa City, Iowa underwent our assessment as pilot subjects. Individuals who were eligible for participation in our overall study were not eligible to serve as pilot subjects. This pilot testing provided information on how to structure and streamline the proposed assessment, and to determine the optimal phrasing of questions in the evaluation. In addition, the pilot subjects provided important feedback on how to make the assessment as convenient and comfortable as possible for research participants.

The data gathered in the pilot phase were used to test the data management systems that were developed for this study. The pilot data will not be used in study-related analyses, but afforded an opportunity to test data collection and entry. Based on this experience, minor modifications were made to facilitate data entry, organization of the evaluation and to maximize data security and confidentiality.

Data Collection

As the pilot testing concluded, we began recruiting research subjects. The first research subject was assessed on 1 March 1999. Through September 1999, the end date of the second year period, 155 assessments have been completed (see Table 1 and Appendix A for more information on these subjects).

Instrument Revision

After reviewing the assessment's battery of questionnaires, the study group determined that it would be beneficial to include some additional instruments. The Disability and Distress Rating instrument was added to the physical assessment to provide a clinician's judgment of the level of physical disability and psychological distress exhibited by research subjects. A 10 cm. visual analog scale rating current pain (based on Huskisson's pain scale) was also added, as was the Dartmouth COOP charts for Primary Care Practice as an assessment of general health and functioning. The Barsky Amplification Scale was added to get a direct assessment of amplification of symptoms; the Anxiety Sensitivity Index (ASI) provides further assessment of this construct. The Whitley Index assesses hypocondriasis.

Based on ongoing reviews of the study design, data collection, and initial evaluations of subjects, a number of questions have been added to the assessment to help address important research questions that had not been previously considered. These are presented in Appendix B. First, it was determined that knowledge of subjects' current military status (e.g., active, reserve, discharged, retired, etc.) at the time of the evaluation would be useful in future analyses. With the help of Col. Mark Zirkelbach of the lowa Army National Guard, we developed a new item to assess this issue. We also determined that information regarding subjects' current physical fitness activities and self-assessed level of physical fitness would be useful as another self-assessed measure of health status, so a series of seven questions to address this topic were added. Four questions were added to explore subjects' sources of medical information. These questions also will be useful when analyzing recently added openended questions that address sources of information specifically on Persian Gulf War illness.

One major accomplishment of the past year was the development of a qualitative analysis component to the study. This facet of the study has four basic aims: 1) to understand the experience of illness and care received by those with medical problems; 2) to determine sources of information regarding PGW illness; 3) to examine for a possible media effect on symptom reporting; 4) to better understand subjects' perceptions of PGW illness and concerns. In this component subjects are asked a series of structured open-ended questions that assess what measures were taken to prepare troops for the Gulf War, the existence of problems that the individual attributes to service during the period of the Gulf War, and the routes through which subjects get information about illness in Gulf War veterans.

Table 1. Subjects Assessed Through 30 September 1999 (n=155)

	Number	Percent
Exposure status		
PGW	105	67.7
non-PGW	50	32.3
Military status		
Regular military	37	23.9
National Guard/Reserve	118	76.1
Gender		
Male	148	95.5
Female	7	4.5
Race		
White	152	98.1
Black/other	3	1.9
Branch		
Army	118	76.1
Air Force	7	4.5
Marines	15	9.7
Navy/Coast Guard	15	9.7
Rank		
Enlisted	146	94.2
Officer	9	5.8
State of residence		
lowa	142	91.6
Illinois	5	3.2
Missouri	4	2.6
South Dakota	2	1.3
Minnesota	1	0.7
Nebraska	1	0.7
Wisconsin	0	0.0
Age		
Mean	41.4	
Std. Dev.	9.5	
Minimum	27.7	
Maximum	71.0	

Characteristics of Subjects Assessed to Date

Through 30 September 1999, a total of 155 subjects had been assessed, and another 68 had scheduled assessments. Thus far, 76 subjects have declined, for an acceptance rate of 74.6%. The main reasons given for declining are travel distance and work schedule. We are collecting structured information on reasons for declining to participate, which will be reported once the study is completed.

Among those evaluated to date, deployed subjects total 105, with non-deployed subjects accounting for the other 50 assessments completed. Of the 155 subjects assessed, 124 are cases, while the remaining 31 did not meet the definition for cognitive dysfunction, depression, or fibromyalgia. Appendix A presents a breakdown of subjects assessed to date by outcome and deployment status. Table 1 shows descriptive data on these study participants.

Data Analysis/Publication

Data collected as part of the ongoing evaluation for this study have yet to be presented to the public. However, a number of papers and presentations have been developed recently by members of the research team that examine a variety of PGW-related research questions, or utilize data from this study population. A list of these works is shown in Appendix B.

Personnel

The study is fully staffed. Appendix C depicts the personnel associated with the project.

Research Methods

Throughout the past year, we have continued to hold bimonthly study group meetings. These provide all research and scientific personnel involved in the project the opportunity to discuss study recruitment and scheduling, theoretical and methodological issues, and any other topics related to the study. This forum has proven valuable for refining the research questions and for addressing practical questions regarding research procedures and methodology. We also hold regular weekly and *ad hoc* meetings of key personnel to address specific considerations, such as recruitment and subject location, assessment of interobserver reliability, data security and database issues, and other issues relevant to the successful completion of the study. A detailed list of the revised instruments and assessments used in this study is presented in Appendix D.

In addition to the primary data that will be generated in this project, we will utilize secondary data to assess pre-deployment health status variables, as well as post-deployment data associated with our research subjects. We have been working with the Defense Manpower Data Center (DMDC) to secure access to data relevant to this project. These data will include variables collected at enlistment and throughout an individual's military career. This information will help in a variety of analyses, including the assessment of pre-existing states/conditions, aid in controlling for pre-deployment health status, and as a validity check for a variety of self-reported variables.

We are using the facilities of the University of Iowa Health Care's (UIHC) General Clinical Research Center (GCRC) for the assessments. These facilities provide an optimal clinical research setting for the project and allow a "subject-centered" research assessment – instead of transporting subjects to different parts of the hospital to undergo the various facets of the assessment, subjects are centrally located in the GCRC throughout the assessment day. Subjects are provided lunch in the GCRC cafeteria and, if desired, subjects can spend the night in a GCRC inpatient room. In addition, experienced GCRC nursing staff obtain vital signs and perform phlebotomy.

Research Subjects

Subjects have been selected from the persons who participated in the Iowa Persian Gulf War study (n=3,695). To limit the pool of subjects to those who would be likely to participate, which involves travel to Iowa City for an in-person evaluation, the pool has been selected to include telephone survey participants whose last known address was in Iowa or a bordering state. The total number of eligible subjects in these states, referred to as "the surrounding region" is 2,464. Appendix E shows these subjects in the surrounding region by deployment status and the study's three *a priori* outcome categories (based on self-report data from the telephone survey).

Each subject falls into one of eight categories, reflecting the seven possible combinations of the three *a priori* outcomes of interest, as well as a category for those who do not meet the criteria for any of the three outcomes. A "case" is an individual who, based on the telephone survey, meets the criteria for one or more of the following *a priori* outcomes: cognitive dysfunction, fibromyalgia, and/or depression. A control subject is an individual who did not meet the definition for any of these three *a priori* outcomes, based on the self-report data. Subjects are also categorized reflecting whether or not they were deployed to the Persian Gulf theater during the PGW era. The resulting number of subjects in each group is shown in Table 2.

As table 2 shows, among the cases, deployed subjects outnumber non-deployed subjects for all but one of the combinations ("depression only" is the exception). To yield maximum precision in the estimate of the false positive rate of symptom reporting, it was decided to sample deployed to non-deployed subjects in an approximate 2 to 1 ratio. Because of the relatively small numbers of non-deployed cases, we are attempting to recruit all the non-deployed cases in any of the seven combinations of outcomes; we have randomly selected twice this number of deployed cases. If fewer than twice as many deployed as non-deployed subjects are available for a given outcome combination, all the deployed subjects for that stratum will be recruited.

There will be two exceptions to the 2 to 1 ratio of deployed to nondeployed. First, we plan to include all 85 of the deployed cases who met the case definition for cognitive dysfunction. Cases who met the definition for cognitive dysfunction, but not the criteria for the other two study conditions are of particular importance. Therefore, the decision was made to include the 25 deployed cases with only cognitive dysfunction and who would have been excluded by strict adherence to the 2 to 1 ratio. All 58 of the deployed cases who met the *a priori* case definition for both cognitive dysfunction and fibromyalgia have been included. Strict adherence to the 2 to 1 ratio would lead to only 18 deployed cases with this combination of conditions in the sample. In order to fully characterize those with reports of cognitive dysfunction, it was decided to include all 58 deployed cases who met the case definition for this outcome combination.

Table 2. Total Cases and Controls Available for Assessment, Desired Sample Sizes, and Completed Subjects by *A Priori* Outcome Group Combinations*

		J	Not Deploy	yed		Deploye	d		Total	
			Desired			Desired			Desired	
	A Priori Outcome Groups	Total	Sample	Complete	Total	Sample	Complete	Total	Sample	Complete
	Cognitive Dysfunction, Fibromyalgia, and Depression	28	28	6	82	56	6	110	84	12
	Cognitive Dysfunction and Fibromyalgia	9	9	3	58	58	14	67	67	17
Cases	Cognitive Dysfunction and Depression	32	32	3	65	64	7	97	96	10
	Cognitive Dysfunction only	30	30	4	85	85	20	115	115	24
	Fibromyalgia and Depression	20	20	5	30	30	5	50	50	10
	Fibromyalgia Only	87	87	14	130	130	22	217	217	36
	Depression Only	51	51	6	48	48	9	99	99	15
	Subtotal of cases	257	257	41	498	471	83	755	728	124
Controls	None of the three conditions ¹	919	100	9	791	200	22	1,710	300	31
Totals		1,176	357	50	1,289	671	105	2,465	1,028	155

^{1.} Neurocognitive evaluation to be completed on approximately 100 deployed controls and 100 non-deployed controls.

Total Number of Eligible Cases² for Each A Priori Outcome Group

	Not Deployed	Deployed	Total
Eligible Cognitive Dysfunction Cases	99	263	362
Eligible Fibromyalgia Cases	144	234	378
Eligible Depression Cases	131	198	329

^{2.} Subjects meeting the case definition for each of the three *a priori* illness outcomes based on the telephone survey; the sum of these numbers is greater than the total number of cases due to overlap among subjects in the three illness groups.

^{*}Note: data complete as of September 30, 1999.

Cases are also of central importance for those analyses addressing the characteristics of illness among deployed individuals and identifying their associated risk factors. To maximize precision when addressing these questions, it was decided to sample cases to controls at an approximately 2 to 1 ratio.

As shown in Table 2, this approach yields a total of 728 deployed and non-deployed cases for potential inclusion in the study. Since the participation rate will be less than 100%, we expect approximately 630 of these subjects to participate.

As seen in Table 2, this sampling plan would yield a maximum of 257 non-deployed cases, and 471 exposed cases, for a total of 728 cases. The addition of 300 control subjects yields a total of 1,028 subjects for the initial contact pool.

To help ensure comparability across cases and controls, we are utilizing an adaptive randomization approach. While retaining the element of random selection, this approach yields a somewhat higher probability of inclusion for control subjects, who are similar to subjects in the case group on characteristics likely related to outcome, e.g., age, race, gender, officer/enlisted status, and branch of service. Adaptive randomization procedures adjust the allocation probabilities of subjects as a study progresses (see *Fundamentals of Clinical Trials* by Friedman, Furberg, and DeMets for a discussion of the concept). As we drew our sample of cases, we adjusted the probability of selection of control subjects who were similar with regard to the demographic and service-related variables listed above. Subjects were not matched on these characteristics per se, but the probability of being selected for subjects within the control group that were more similar to the cases than other potential controls on certain key stratification variables that were likely confounders was increased.

A major consideration for this study is locating and contacting potential research subjects. Several years have passed since the telephone survey, and a large number of subjects have relocated in the meantime. Once the sample for the present study was identified, the following steps have been taken to maximize the probability of locating and contacting the largest possible number of subjects. First, an introductory letter was sent to subjects' last known address. The letter discussed the current study and instructed subjects on how to contact the project via a toll-free number should they have questions, or if they would like to set up an appointment. Included with this letter was a return postcard to allow subjects to make any necessary corrections to their address and phone number, and to list the best times for telephone contact. If a subject returned the postcard with contact instructions, follow-up was made per those instructions. If no specific callback date was noted, contact was made as soon as possible after receiving the postcard.

In many cases the original introductory letter was returned by the post office as undeliverable. Sometimes a label would be affixed to the envelope listing the subject's current address, and in these cases a new letter was issued to that address. Nore

commonly, a letter was returned with no current address listed. When this happened several Internet services were used to try to determine the subject's current address. If this failed to produce any leads, a telephone call was placed to the permanent contact person the subject listed in the previous telephone survey

The permanent contact person has been a valuable tool for locating a large number of subjects. In instances when the permanent contact person is not available, or is not able or willing to provide updated information on a potential subject, the search for the subject has been outsourced to ChoicePoint (formerly Equifax), a credit agency search firm that specializes in locating individuals. The first batch of outsourced names was recently returned, and new introductory letters were mailed to these individuals the second week in October, 1999. Any subjects who are still unaccounted for after a search by ChoicePoint will be designated "currently unable to contact." Subjects with this designation will be reviewed on a monthly basis throughout the subject accrual phase of the study to consider new subject location approaches on an ongoing basis.

Schedule

We have been scheduling subjects at a convenient time up to several months into the future. Currently, we have approximately 10-12 subjects scheduled per week for the next month, with fewer subjects currently scheduled further into the future. Assuming an average of just under 2 subjects assessed per day, the subject assessment phase of the study should end no later than March 2001. An effort is being made to assess 3 subjects per day as often as possible; maintaining an average of 2.8 subjects assessed per day would give an estimated completion date for the subject assessment phase of the project at September 2000. This also assumes that we are able to contact and schedule subjects with approximately the same relative effort, which may not be true as we progress to more difficult to reach subjects.

Data Management

Study data are being entered on an ongoing basis. A number of steps have been taken to ensure data accuracy and quality. First, all data are being entered on electronic forms that have built-in range checks – for example, if a specific item only has a valid range of 1 through 5, the form is set up to accept input only within this range. The forms are also set up to bear a close resemblance to the original instruments from which the data are coded. To help ensure the accuracy of data entry, two different data entry personnel are entering the data twice. The second entry is compared to the first, and any discrepancies are resolved. Discrepancies that cannot be easily resolved, i.e., that are due to an ambiguous response by the subject or something else beyond a simple keystroke error, are reviewed by the study coordinator and, if necessary, by the principal investigator. If the response is still unclear the study coordinator will contact the subject for clarification.

As noted, data entry has been in progress since the subject assessment phase of the project began. To date, data for each assessed subject have been entered once, and the second entry has been completed for approximately one-third of these subjects.

Conclusion

The project is fully staffed and subject accrual and assessment are ongoing. Recruitment and assessment processes are being constantly assessed for opportunities to increase efficiency and effectiveness. The project is on track to finish subject accrual 6 to 12 months before the end of the grant period. In the meantime, analyses will be planned and statistical analysis programs will be developed in advance to allow the most productive use of the months between the end of subject accrual and the end of the grant period. Also, in an effort to maximize the efficient use of the rich database that is being developed as part of this study, the research team will work to develop interim analyses that could lead to papers and presentations of interest even before subject accrual is complete.

Appendix A. Completed Assessments Broken Down by *A Priori* Outcome and Deployment Status (Assessments completed through 9/30/99)

Cognitive Dysfunction

	Deployed	Not Deployed	
Symptomatic ¹	47	16	
Not Symptomatic	58	34	
	105	50	155

Depression

	Deployed	Not Deployed	
Symptomatic	27	20	
Not Symptomatic	78	30	
	105	50	155

Fibromyalgia

1 1010111741914			
	Deployed	Not Deployed	
Symptomatic	47	28	
Not Symptomatic	58	22	
	105	50	155

By Illness Combinations

							CD,		
				CD,	CD,	Dep,	Dep,	No	
	CD	Dep	Fibro	Dep	Fibro	Fibro	Fibro	Illness	Total
Deployed	20	9	22	7	14	5	6	22	105
Not Deployed	4	6	14	3	3	5	6	9	50
Total	24	15	36	10	17	10	12	31	155

¹ For each outcome, refers to self-reported symptomatology based on the 1995-96 telephone survey

Appendix B. Recent PGW-Related Papers and Presentations

Peer-Reviewed Papers Published or In Press:

Black, D.W., Doebbeling, B.N., Voelker, M.D., Clarke, W.R., Woolson, R.F., Barrett, D.H., and Schwartz, D.A. Quality of life and health service utilization in a population-based sample of military personnel reporting multiple chemical sensitivities. J. Occup. Environ. Med. 41(10):928-933, 1999.

Black, D.W., Doebbeling, B.N., Voelker, M.D., Clarke, W.R., Woolson, R.F., Barrett, D.H., and Schwartz, D.A. Multiple Chemical Sensitivity Syndrome: Symptom Prevalence and Risk Factors in Gulf War Veterans and Comparable Controls. Arch. Intern. Med. (In press), 1999.

Abstracts:

Doebbeling, B.N., Rohrer, J.E., Woolson, R.F., Torner, J.C., Saag, K.G., Merchant, J.A., Bentler, S., and Schwartz, D.A.: Health Services Utilization among Persian Gulf War and Activated Non-deployed Veterans. Annual Meeting of the American Public Health Association, Indianapolis, IN, p. 123, November 11, 1997.

Doebbeling, B.N., Woolson, R.F., Torner, J.C., Merchant, J.A., Barrett, D., Polzer, J.P., and Schwartz, D.A.: Self-reported Illness Following Service in the Persian Gulf: Multiple Medical Conditions. Annual Meeting of the American Public Health Association, Indianapolis, IN, p.5, November 10, 1997.

Voelker, M., Doebbeling, B.N.: Predictors of Mental Health Service Utilization Among Persian Gulf War Veterans. Abstracts of the 1997 International Conference on Health Policy Research: Methodologic Issues in Health Services and Outcomes Research. Boston, MA, December 1997.

Zwerling, C., Torner, J.C., Clarke, W.R., Voelker, M.D., Doebbeling, B.N., Barrett, D.H., Merchant, J.A., Woolson, R.F., and Schwartz, D.A.: Traumatic Injury Among Gulf War Era Veterans: An Analysis of the Iowa Persian Gulf War Study. 31st Annual Meeting of the Society for Epidemiologic Research, Chicago, IL, June 24-26, 1998.

Carney, C.C., Allen, J., Clarke W; Schwartz, D.A., Woolson, R., Barrett, D., and Doebbeling, B.N.: Gender Differences in Health Status in a Population-Based Sample of Military Personnel Deployed or Activated, Not Deployed to the Persian Gulf. 45th Annual Meeting of the Academy of Psychosomatic Medicine, Psychosomatics, November 1998.

Voelker, M.D., Torner, J., Woolson, R., and Doebbeling, B.N. Symptomatology Associated With Self-Perceived Health Decline among Gulf War Veterans and Era Controls. Abstracts of the Federal Investigators Annual Meeting on Persian Gulf War Illness, Washington, DC, June 23-25, 1999.

Simms, L. J., & Watson, D. (1999, August). Exploratory factor analysis of PTSD symptoms in two military samples. Poster presented at the 107th Annual Convention of the American Psychological Association, Boston, MA.

Other: Exhibits, Films, Tapes, Special Presentations:

"The Iowa Persian Gulf Study: An Update," Institute of Medicine/National Academy of Sciences, Committee on the Health Effects Associated with Exposures Experienced During the Gulf War, Georgetown, June 14, 1999.

"Case Definition Panel Discussion" Scientific Discussant, 4th Annual Meeting of Federal Investigators on Gulf War Illness, Washington, DC, June 23, 1999.

"Veterans' Forum: A Roundtable Discussion," Scientific Discussant, 4th Annual Meeting of Federal Investigators on Gulf War Illness, Washington, DC, June 24, 1999.

Papers Submitted:

Doebbeling, B.N., Clarke, W.R., Watson, D., Torner, J.C., Woolson, R.F., Voelker, M.D., Barrett, D.H., and Schwartz, D.A. Is There a Persian Gulf War Syndrome? Results from a Large, Population-based Study. (Submitted), 1999.

Zwerling, C., Torner, J.C., Clarke, W.R., Voelker, M.D., Doebbeling, B.N., Barrett, D.H., Merchant, J.A., Woolson, R.F., and Schwartz, D.A. Self-Reported Injuries Among Gulf War Veterans: A Population-based Study. (Submitted), 1999.

Barrett, D.H., Voelker, M.D., Doebbeling, B.N., Falter, K., Kathol, R., Woolson, R.F., and Schwartz, D.A. Post-traumatic Stress Disorder and Physical Health Status among U.S. Military Personnel Serving During the Gulf War Period: A Population-based Study. (Submitted), 1999.

Appendix C. Study Personnel

Principal Investigator:	Bradley Doebbeling, MD, MSc
Co-Investigators:	Joseph Barrash, PhD
	Donald Black, MD
	Gwendolyn Ford, MD
	Kenneth Saag, MD
	David Schwartz, MD
	Robert Woolson, PhD
	Thoru Yamada, MD
Study Coordinator:	John Holman, MA
Senior Programmer Analyst:	Mary Howard, MA, MS
Physical Examiners:	Dina Janzen, MD
	Robert Zwicki, DO
Research Assistant:	Megan Adams, BA, BS
Research Assistant (Neurology):	Amy Schumacher, MS
Student Research Assistants:	Carolyn Freese
	Katie Russell
	Jane Zingler

Note: Several additional investigators have been regular participants in the study group, making regular contributions to the study and participating out of personal or scientific interest. These include two of our consultants and multiple other investigators: Drs. David Watson, PhD, Psychology, James Torner, PhD, Epidemiology, Arthur Hartz, MD, PhD, Family Medicine, Caroline Carney, MD, Internal Medicine/Psychiatry, Margaret Voelker, PhD, Epidemiology, and Susan Zickmund, Internal Medicine.

Appendix D. Data Collection Instruments 1. NEUROPSYCHOLOGICAL BATTERY

Test/Item	Abilities assessed
Background Interview	Academic/neurologic history
WAIS-R Similarities	Verbal intellect
WAIS-R Block Design	Nonverbal intellect, visuoconstruction
WAIS-R Digit Span	Concentration, immediate memory span
WAIS-R Digit Symbol	Nonverbal learning, visuomotor speed
NART-R	Premorbid intelligence
COWA	Expressive language, sustained attention
Rey AVLT	Verbal learning and memory
AVLT-Repeated Delay	Exaggeration
BVRT	Immediate visual, memory, exaggeration
RMT	Verbal memory, visual memory, exaggeration
Stroop Test	Response inhibition, concentration
Trail Making Test	Visual scanning, visuomotor speed, cognitive shifting
Starry Night Test	Reaction time, sustained visual attention
Grooved Pegboard Test	Manual dexterity, visuomotor integrity
MMPI-2	Psychological status, exaggeration

NART-R = National Adult Reading Test-Revised; COWA = MAE Controlled Oral Word Association Test; Rey AVLT = Rey Auditory Verbal Learning Test; BVRT = Benton Visual Retention Test; RMT = Warrington Recognition Memory Test; MMPI-2 = Minnesota Multiphasic Personality Inventory-2.

2. MENTAL HEALTH EXAMINATION

Instrument	How Administered	Assesses	
SCID-IV	rater	Axis I disorders	
GAS	rater	Global function	
BLSQ	self-report	Life Stress	
Mississippi Scale	self-report	PTSD symptom severity, effects	
SPS	self-report	Social support	
Barsky Amplification Scale	self-report	Amplification	
ASI	self-report	Amplification; Hypocondriasis	
Whiteley Index	self-report	Amplification; Hypocondriasis	
MASQ	self-report	Mood and Anxiety	
SNAP	self-report	Personality	

SCID-IV = Structured Clinical Interview for DSM-IV Non-Patient Version; GAS = Global Assessment Scale; BLSQ = Brief Life Stress Questionnaire; SPS = Social Provisions Scale; MASQ = Mood and Anxiety Symptom Questionnaire; SNAP = Schedule of Nonadaptive and Adaptive Personality

3. PATIENT EVALUATION

Instrument	How Administered	Evaluation
History and Physical form	Clinician	History and Physical
Review of Systems form	Clinician	Review of Systems
Family History form	Clinician	Family History
Disability and Distress		Physical Disability and
Rating	Clinician	Psychological Distress
SF-36	Self-report	Health Status
Health Utilities Index	Self-report	Health Status, Utility Measure
Dartmouth COOP Charts	Self-report	Health Status, Health Functioning
10 cm. Visual Analog Pain		
Scale	Self-report	Current Pain
Occupational Exposure questionnaire	Self-report	Occupational Exposure

Appendix E. Eligible Subjects (based on the study's three *a priori* outcomes) Potential Subjects for Cognitive Dysfunction Study

	Symptomatic	Not Symptomatic	Total
Exposed	290	999	1289
Not Exposed	99	1076	1175
Total	389	2075	2464

Potential Subjects for Depression Study

	Symptomatic	Not Symptomatic	Total
Exposed	225	1064	1289
Not Exposed	131	1044	1175
Total	356	2108	2464

Potential Subjects for Fibromyalgia Study

	Symptomatic	Not Symptomatic	Missing	Total
Exposed	300	989		1289
Not Exposed	144	1030	1	1175
Total	444	2019		2464